

Validation data for TDI-6570

<https://www.invivogen.com/tdi-6570-cGAS-inhibitor>

For research use only

Version 24C25-AK

TDI-6570 is a small molecule inhibitor of the cytosolic double-stranded DNA sensor cyclic GMP-AMP synthase (cGAS). TDI-6570 has been shown to have a dose-dependent inhibitory activity on mouse cGAS-induced IRF signaling pathways, as assessed using InvivoGen's J774-Dual™ cell line (Figure 1). As expected, TDI-6570 is highly specific for mouse cGAS with no noted off-target effects on other cytosolic sensors, such as on the 2'3'-cGAMP-induced STING. Moreover, TDI-6570 has no inhibitory effect on human cGAS signaling, as verified by using the human monocytic THP1-Dual™ cell line, compared to G140, a potent human cGAS inhibitor (Figure 2).

Specific inhibition of mouse cGAS in J774-Dual™ cells

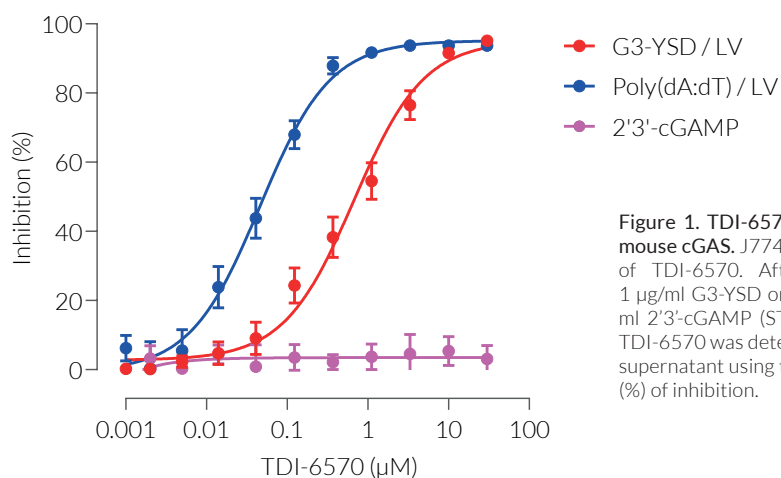


Figure 1. TDI-6570 is a potent inhibitor of the IRF signaling pathway downstream of mouse cGAS. J774-Dual™ cells were cultured in the presence of increasing concentrations of TDI-6570. After 3 hours of incubation, the following ligands were added: 1 μg/ml G3-YSD or Poly(dA:dT) (cGAS agonists), complexed with LyoVec™ (LV), or 10 μg/ml 2'3'-cGAMP (STING agonist). After overnight incubation, the neutralizing activity of TDI-6570 was determined by measuring the reduction of Lucia luciferase production in the supernatant using the QUANTI-Luc™ 4 detection reagent. Data are shown as a percentage (%) of inhibition.

Effect of TDI-6570 on human cGAS in THP1-Dual™ cells

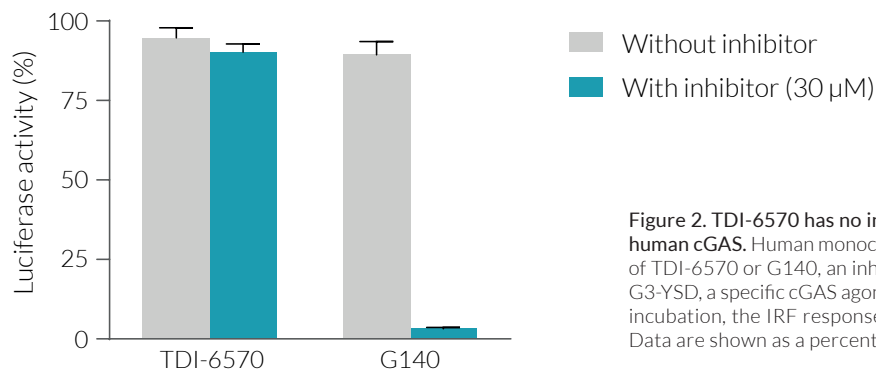


Figure 2. TDI-6570 has no inhibitory effect on the IRF signaling pathway downstream of human cGAS. Human monocytic THP1-Dual™ cells were cultured in the presence of 30 μM of TDI-6570 or G140, an inhibitor of human cGAS. After 3 hours of incubation, 1 μg/ml of G3-YSD, a specific cGAS agonist, complexed with LV, was added to the cells. After overnight incubation, the IRF response was assessed using the QUANTI-Luc™ 4 detection reagent. Data are shown as a percentage (%) of maximal IRF-induced Lucia luciferase activity.

TECHNICAL SUPPORT

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